

SHORT COMMUNICATION

The essential role of Broca's area in imitation

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Abstract

The posterior sector of Broca's area (Brodmann area 44), a brain region critical for language, may have evolved from neurons active during observation and execution of manual movements. Imaging studies showing increased Broca's activity during execution, imagination, imitation and observation of hand movements support this hypothesis. Increased Broca's activity in motor task, however, may simply be due to inner speech. To test whether Broca's area is essential to imitation, we used repetitive transcranial magnetic stimulation (rTMS), which is known to transiently disrupt functions in stimulated areas. Subjects imitated finger key presses (imitation) or executed finger key presses in response to spatial cues (control task). While performing the tasks, subjects received rTMS over the left and right pars opercularis of the inferior frontal gyrus (where Brodmann area 44 is probabilistically located) and over the occipital cortex. There was significant impairment in imitation, but not in the control task, during rTMS over left and right pars opercularis compared to rTMS over the occipital cortex. This suggests that Broca's area is a premotor region essential to finger movement imitation.

Introduction

In this article, we address the significance of increased activity in Broca's area during non-language tasks, specifically during imitation (Hauser *et al.*, 2002). In principle, any increased activity of language-related brain areas during a non-language task may be due to inner speech that may even occur in absence of subject's awareness (Grezes & Decety, 2001; Heyes, 2001). The theoretical import of this problem is clear: is language encapsulated, thus requiring dedicated neural structures (Chomsky, 1986) or not? Lesions in Broca's area are associated with a specific language disorder (Broca's aphasia), characterized by a deficit in speech output and somewhat preserved language comprehension (Geschwind, 1970). Also, direct cortical stimulation of pars opercularis of the left inferior frontal gyrus (the posterior sector of Broca's area) in awake neurosurgical patients, produces speech arrest (Ojemann, 1979). In addition to speech, Broca's area is activated in several linguistic tasks (Bookheimer, 2002), among them syntax processing, which seems to specifically activate the posterior sector of Broca's area, the pars opercularis (Dapretto & Bookheimer, 1999). Taken together, the available evidence makes Broca's area a plausible candidate for a brain region exclusively dedicated to language processing.

There is also evidence, however, that Broca's area activity is increased in several motor tasks involving the execution, imagination, imitation and observation of finger movements (Grafton *et al.*, 1996; Krams *et al.*, 1998; Iacoboni *et al.*, 1999; Binkofski *et al.*, 2000). In addition, comparative neuroanatomy considerations suggest that a sector of Broca's area, Brodmann area 44, evolved from area F5 of the macaque brain (von Bonin & Bailey, 1947; Petrides & Pandya, 1994; Rizzolatti & Arbib, 1998). In the area F5 region, there are 'mirror' neurons activated by the execution of an action and by the observation of the same action performed by somebody else (di Pellegrino *et al.*, 1992; Gallese *et al.*, 1996). This 'mirror' neural system may have been an essential neural system for the evolution of social communication. The creation of an internal copy of an observed action that is largely indistinguishable from an action performed by the self places the observer in the perspective of the actor. It could allow the observer to recognize the actions of others in a non-inferential fashion. Similarly, the neural map of an action creates a common link between the actor and the observer. Such neural equivalence between the sender and receiver of a message is felt to be a requisite of communication (Lieberman & Mattingly, 1985; Lieberman & Whalen, 2000; Fadiga *et al.*, 2002). Thus, there is a plausible alternative to the account of a 'language-dedicated' area that explains the involvement of Broca's area in language processing. Broca's area may be a non-inferential, non-symbolic motor region with 'mirror' neural properties that are critical to action understanding and to imitation. More complex functional properties that are inherent to language may have been

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built upon this relatively simple neural mechanism that facilitates communication between individuals.

We have approached the problem of the role of Broca's area in imitation using repetitive transcranial magnetic stimulation (rTMS). This technique allows the transient disruption of normal functions in stimulated brain region, thus creating a 'virtual' lesion that temporarily mimics the effects of brain lesions (Hallett, 2000; Walsh & Cowey, 2000). The prediction is straightforward. If the increased activity in Broca's area during imitation of finger movements is only an epiphenomenon due to inner speech, and perhaps subconscious, then rTMS over Broca's area should not interfere with the imitative process. If, in contrast, the neural activity in Broca's area is essential for imitation, a 'virtual' lesion in Broca's area should result in a deficit in imitation.

Methods

Subjects

We studied eight, right-handed (as assessed by a modified Oldfield Handedness Questionnaire) (Oldfield, 1971) healthy volunteers (6 males, 19 to 34 years) with normal to corrected to normal vision. Subjects were naive to the purpose of the study. The subjects were screened to rule out a history of neurological, psychiatric and medical problems, and contraindications to TMS. A brief neurological exam was also performed on each subject. The study was approved by the UCLA Institutional Review Board and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Written informed consent was obtained from all subjects prior to the inclusion in the study.

Experimental tasks

A visual description of the two tasks is provided in Fig. 1. The leftmost and the rightmost keys were never pressed and the thumb was never used in both tasks. The starting position of the hand in both tasks was such that the index finger was placed behind the second key from the left, the middle finger was placed behind the third key from the left and so on.

Imitation task

Our stimulus set consisted of 160 different digital video clips of a hand pressing a sequence of 2 of 4 possible keys on a key-press box. The sequence of finger movements in each video clip consisted of the

following: the actor lifted one finger from a resting position and placed that finger on a key (key-press 1). The actor then moved the same finger from the first key onto a second key or, in some clips, simply lifted the finger and replaced it back onto the same key (key-press 2). After the second key-press, the actor moved the finger back to its original resting position. Each trial consisted of one video clip. The amplitude and velocity of the finger movement varied from trial to trial. No trial was repeated within an experiment. Trials lasted from 1825 ms to 5865 ms. Inter-trial interval was 200 ms. At each stimulation site, subjects performed 2 blocks of 20 different trials (40 trials total per stimulation site), with a five-minute rest between blocks. Thus, there were 120 different imitation trials per subject. A subset of clips, (40 of the total 160 clips), were used for the subjects to practice the task leaving 120 novel clips for the experiment.

Subjects were instructed to imitate the finger movement simultaneously with the movement shown. After each trial, the subject returned to the original starting position using markers located behind each of the four keys that were used in the experiment (keys 2–4 on the keyboard). Subjects' hands were positioned in such a way that they could see their hand and use visual information to guide their movements back to the start position. Subjects used their right hand.

Control task

In this task a moving red dot was presented instead of a finger. The red dot would appear over a sequence of two out of 4 possible keys. The leftmost and the rightmost keys were never used, as in the imitation task. Subjects were instructed to move the finger that matched the spatial starting position of the moving red dot in each trial and begin their movement as soon as the red dot appeared. For example, if in a given trial a red dot appeared on the second key from the left, subjects used their index finger in that given trial. All the remaining parameters (total number of trials, 120; practice trial, 40; intertrial interval, duration of the trials, number of trials per block, number of blocks, interblock interval) were identical to the imitation task.

TMS protocol

Subjects were seated in front of a computer monitor 57 cm away during the experiment. A custom-made forehead and chin rest, which was fixed to a coil-holder, was used to minimize head motion. Locations for TMS were determined by collecting T1 magnetic resonance (MR) images on each subject. MR images were acquired on a 3 Tesla General Electric scanner with a 1 NEX 3D spoiled grass sequence

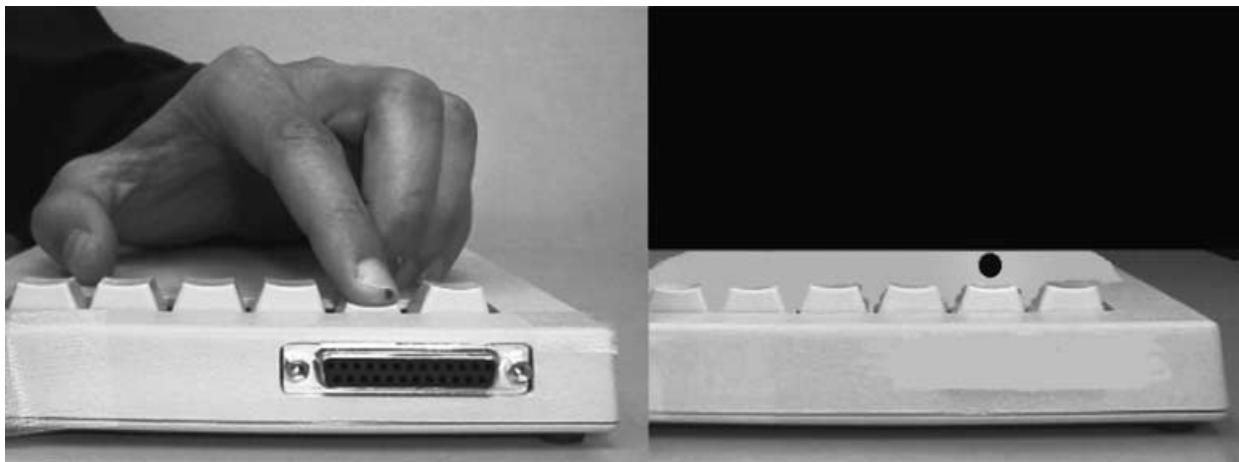


FIG. 1. Left (imitation task): subjects were shown a sequence of finger movements pressing keys on a keypad and were instructed to imitate the finger movements with their right hand. Right (control task): subjects were shown a moving dot and were instructed to use the right finger corresponding to the starting position of the dot to press the keys on the keypad cued by the moving dot. In the case depicted here, subjects would be using the little finger.

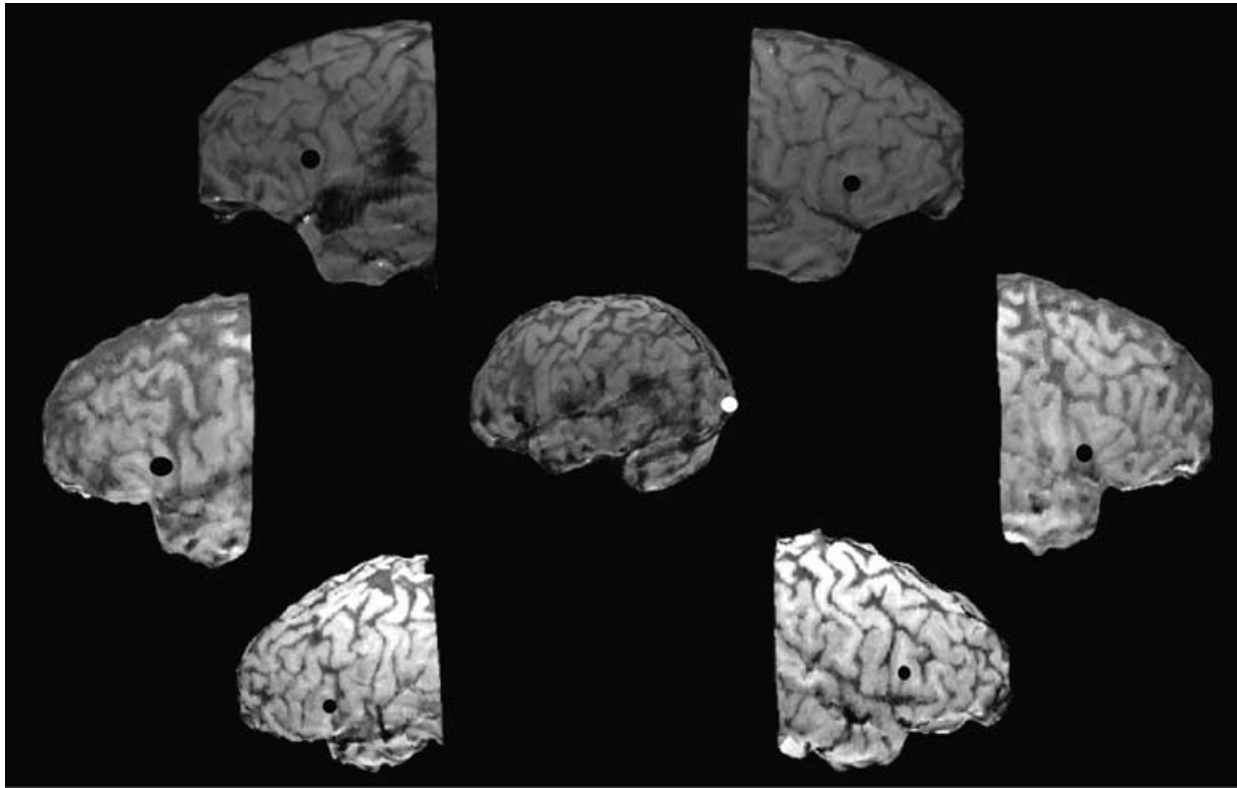


FIG. 2. Surface rendering and target location (black dot) of left and right pars opercularis in three subjects. In the centre of the figure we show a representative target location for the occipital site (white dot).

(TR = 24 ms; TE = 4 ms; FOV = 250 × 250 × 150 mm) prior to the TMS session. The images were reconstructed into surface rendering of sulcal anatomy (BrainSight) and the sites of stimulation were guided by the use of a frameless stereotaxy system (Polaris). The target locations for rTMS were the left (LPO) and right pars opercularis (RPO) of the inferior frontal gyrus, and a medial occipital site (OCC) (see Fig. 2). Repetitive TMS was delivered through a Cadwell High Speed Magnetic Stimulator using a 90-mm angled figure-of-eight coil. The coil was placed such that the maximal induced current flowed in the antero-lateral direction for LPO and RPO, and downward for OCC. The output strength of the TMS was set at 90% of the subject's motor threshold (MT). In one subject, the stimulation intensity was set at 80% of MT since the subject felt uncomfortable at 90%. Motor threshold was defined as the minimal intensity of stimulation capable of inducing motor evoked potentials >50 μ V peak-to-peak amplitude in at least 6 out of 10 trials when applied to the left optimal scalp site. The optimal scalp site was defined as the scalp position and coil orientation from which TMS induced motor evoked potentials of maximal amplitude in the contralateral abductor pollicis brevis muscle. Ten magnetic pulses were applied in two trains of five pulses each with a rate of 5 Hz in every trial of the experiment. The beginning of each train of pulses was synchronized with the beginning of each finger movement in the video clip (imitation task) or with the appearance of each dot within a trial (control task). We did so in light of experimental evidence and theoretical considerations suggesting that movement planning occurs early on (Desmurget *et al.*, 1999; Desmurget & Grafton, 2000). The average MT was 56.8% of maximal output of the stimulator, and the average stimulation intensity during rTMS was 50.3%. All subjects reported similar subjective sensations for all three rTMS sites.

Data analysis

We collected and analysed data regarding four dependent variables. First, accuracy of the key presses (that is, did the subject press the correct key?). This first variable is relevant to the goal of the action to be imitated or performed in the control task. Second, accuracy of finger used to perform the movement (i.e. if a given trial requires the use of index finger, the use of the middle finger would be an error). This second variable is relevant to the process of mapping the visual input onto an appropriate body part for motor output. Third, the time that it took the subject to press each key was compared to the time that it took for the model hand to press each key. This was intended to measure the temporal accuracy of the imitation of the movement. Fourth, the subject's finger movements were recorded on video and the maximum displacement of the finger during a movement was measured and compared to the maximum displacement of the shown finger movement (imitation task) or the maximum displacement of the red dot (control task) from the keyboard. Taken together, the movement time and displacement data provide a quantification of the subject's finger movements.

Note that given our experimental design in which TMS is always applied in every trial, the reported experimental effects rely on comparing the effect of TMS at two different sites and during two different tasks. Thus, our dependent variables are absolute measures, and not percentage changes from a non-TMS baseline.

Data analyses were performed with repeated measures analyses of variance (ANOVAs) on the four dependent variables. Within-subject variables were task (imitation, control) and rTMS target area (LPO, RPO, OCC).

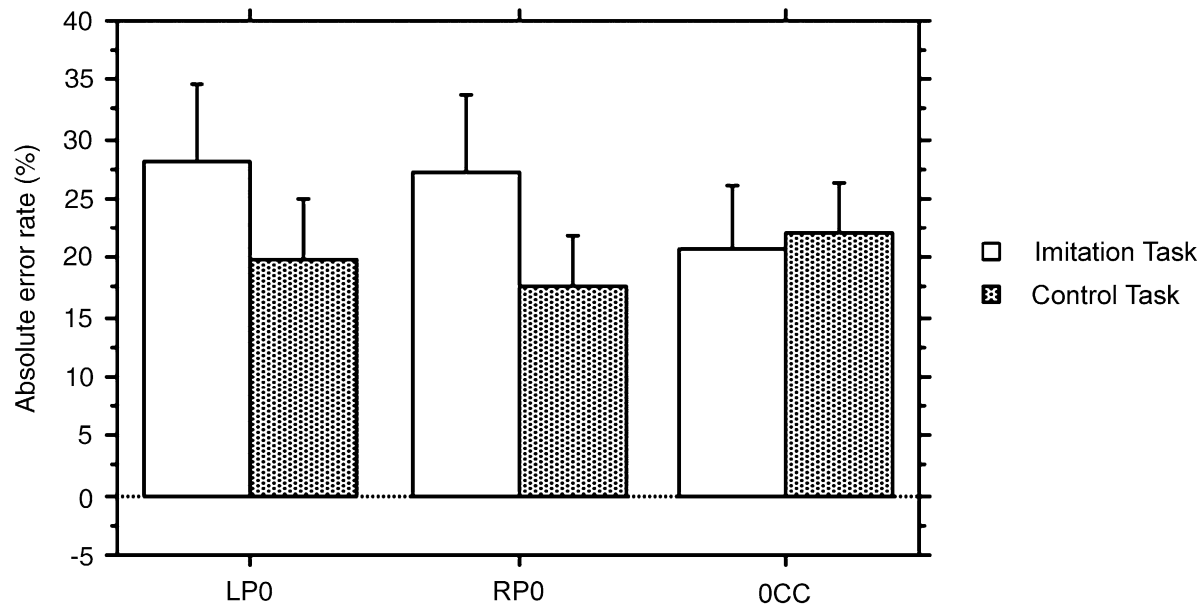


FIG. 3. A 2×3 repeated measures ANOVA on error rate of key presses [two tasks (imitation and control) and three target rTMS areas (LPO, left pars opercularis; RPO, right pars opercularis; and OCC, occipital cortex)], revealed a significant interaction between task and target rTMS area ($F_{2,14} = 3.84$, $P < 0.05$). Planned contrasts revealed that there was a significant difference ($F = 5.77$, $P < 0.04$) in error rates between LPO (28.04%) and OCC (20.73%) during imitation. There was also a significant difference ($F = 4.72$; $P < 0.05$) in error rates between RPO (27.34%) and OCC (20.73%) during imitation. Further, there was a significant difference ($F = 7.25$, $P < 0.02$) in error rates between imitation (28.04%) and control (19.84%) task in LPO. Likewise, there was a significant difference ($F = 10.14$, $P < 0.01$) in error rates between imitation (27.34%) and control (17.66%) task in RPO. No differences in error rates were found between LPO and RPO during imitation and between the three target rTMS areas in the control task. Further, no differences in error rates were found between imitation (20.73%) and control (22.03%) in OCC. Finally, no differences were observed in response times in the two tasks and in all sites.

TABLE 1. Individual percentage errors in imitation and control tasks in the three stimulated sites

Subject number	Individual errors (%)					
	Imitation task			Control task		
	LPO	RPO	OCC	LPO	RPO	OCC
1	55	57.5	50	36.25	37.5	15
2	25	37.5	22.5	13.75	10	13.75
3	17.5	15	7.5	3.75	3.75	13.75
4	25	12.5	12.5	6.25	11.25	22.5
5	56.7	48.7	33.3	20	18.75	18.75
6	7.5	10	2.5	6.25	7.5	10
7	12.5	15	12.5	40	27.5	42.5
8	25	22.5	25	32.5	25	40

LPO, left pars opercularis; OCC, occipital cortex; RPO, right pars opercularis.

Results

The results obtained for accuracy of key presses are shown in Fig. 3. Individual data are presented in Table 1. A task (imitation, control) by target rTMS area (LPO, left pars opercularis; RPO, right pars opercularis; OCC, occipital cortex) repeated measures ANOVA on error rate of key presses revealed a significant interaction between task and target rTMS area ($F_{2,14} = 3.84$, $P < 0.05$). Subsequent analyses revealed that there was a significant difference ($F = 5.77$, $P < 0.04$) in error rates between LPO (28.04%) and OCC (20.73%) during imitation. There was also a significant difference ($F = 4.72$; $P < 0.05$) in error rates between RPO (27.34%) and OCC (20.73%) during imitation. Further, there was a significant difference ($F = 7.25$, $P < 0.02$) in error rates between imitation (28.04%) and control (19.84%) task in LPO. Likewise, there was a significant difference ($F = 10.14$,

$P < 0.01$) in error rates between imitation (27.34%) and control (17.66%) task in RPO. No differences in error rates were found between LPO and RPO during imitation and between the three target rTMS areas in the control task. Further, no differences in error rates were found between imitation (20.73%) and control (22.03%) in OCC.

No significant differences were observed in accuracy of selection of finger used for motor response, in response times, and movement displacement in the two tasks and in all sites.

Discussion

With frameless stereotaxy (Paus, 1999), we were able to visualize precisely the brain region stimulated. Within Broca's area, we targeted its posterior sector, pars opercularis. Recent probabilistic studies mapping cyto-architecture onto brain morphology suggest that, even in presence of large interindividual variability in brain anatomy, the most probable locus of Brodmann area 44 in the human brain is the pars opercularis of the inferior frontal gyrus (Amunts *et al.*, 1999; Mazziotta *et al.*, 2001a; Mazziotta *et al.*, 2001b). We targeted both left and right pars opercularis with rTMS for two reasons. First, in terms of the motor representation of distal body parts in premotor areas, the primate brain seems to show a fairly bilateral organization (Passingham, 1993). Second, a recent analysis of a large functional magnetic resonance imaging (fMRI) dataset performed in our laboratory and including 47 subjects imitating finger movements and 58 subjects observing finger movements had shown bilateral activation of the pars opercularis/Brodmann area 44 (Molnar-Szakacs *et al.*, 2002). We reasoned that, if the left pars opercularis (posterior sector of Broca's area) is activated in imitation tasks because of inner speech, and the right pars opercularis is activated in imitation tasks for reasons more inherently linked to the imitative process, then rTMS on these two brain sites should show differential effects on imitation. If the effect of

rTMS is similar for both left and right pars opercularis, then a similar imitative mechanism in both areas is likely. Finally, as a control site, we also applied rTMS to a brain region not known to show any motor properties, the occipital cortex.

Subjects performed two tasks while receiving rTMS. In one task, the imitation task, subjects imitated a sequence of key presses. They observed a left hand pressing keys while they were using their right hand to imitate the key presses. This configuration of imitation is preferentially observed early in human development (Wapner & Cirillo, 1968) and also yields fewer errors in imitation tasks performed in adults (Ishikura & Inomata, 1995). Thus, the mirror imitative configuration seems the most 'natural' and the less prone to linguistic mediation. In fact, with increasing age, while linguistic competence also increases, the natural tendency to imitate as in a mirror decreases (Wapner & Cirillo, 1968).

There was a selective deficit in the imitation task for rTMS over the left and right pars opercularis (putative Brodmann area 44) of the inferior frontal gyrus, compared to rTMS over the occipital cortex. No differences in performance between the three sites were observed in the control task. There was also a significant difference in error rate between imitation and control task within the left and right pars opercularis. Importantly, in the control site (rTMS over the occipital cortex), no differences were observed in overall performance in the two tasks, suggesting a similar level of difficulty of the two tasks. No effects on the selection of finger used for motor response and movement parameters (temporal delay and movement displacement) were observed between left and right pars opercularis and occipital cortex.

The present results indicate that the posterior sector of Broca's area (pars opercularis) and its homologue in the right hemisphere are essential neural structures for imitation of finger movements. The effect of rTMS on these two brain structures is quantitatively identical, suggesting a common neural mechanism supporting imitation in both left and right pars opercularis. It is unlikely that the effect observed is mediated by a nonspecific motor mechanism (planning, selection, etc.) because rTMS did not produce an effect in the control task which required a very similar motor output and was similar to the imitation task in its difficulty. Thus, in our experiment, rTMS must have interfered with a mechanism within the pars opercularis that is specifically involved in imitation. We suggest that this mechanism is the 'direct matching' mechanism provided by 'mirror' neurons that fire during execution and observation of action (diPellegrino *et al.*, 1992; Gallese *et al.*, 1996; Rizzolatti & Arbib, 1998; Rizzolatti *et al.*, 2001). This mechanism resides, among other regions, in Brodmann area 44 of the human brain (Iacoboni *et al.*, 1999). We previously proposed a 'division of labour' within the frontoparietal network showing 'mirror' properties in the human brain. We suggested that inferior frontal 'mirror' neurons would code the goal of the action to be imitated, whereas parietal mirror neurons would code the motor specification of the action to be imitated (Iacoboni *et al.*, 1999; Iacoboni *et al.*, 2001; Koski *et al.*, 2002; Iacoboni, in press). The present results seem in line with this proposal. The effect observed for rTMS over pars opercularis is confined to the keys to be pressed (the goal of the action) and not to the body part used (the finger selected for motor output) or the temporal and spatial specification of the imitated movement (the detailed motor specification of the movement).

One possible interpretation of this data is that the observed effect is language-mediated such that one has to name the goal of a finger movement in order to imitate it and rTMS interfered with this naming process. This is unlikely, due to at least two major considerations. First, infants can imitate long before they demonstrate any linguistic competence during development (Meltzoff & Moore, 1977) and second, the identical effect for rTMS over the left and right pars opercularis excludes this possibility. Although the right hemisphere has some linguistic competence (Iacoboni & Zaidel, 1996), the left and right pars opercularis differ largely in terms of their language competence, as

clearly shown by neurological (Geschwind, 1970) and neuroimaging evidence (Bookheimer, 2002).

An issue that is worth discussing briefly is the relationships between our bilateral effect and lateralized results obtained in previous TMS studies. Some previous single pulse TMS findings on motor imagery and action observation have yielded somewhat lateralized effects. For instance, single pulse TMS over the left primary motor cortex produces corticospinal facilitation during motor imagery of both left and right hand movements, whereas single pulse TMS over the right primary motor cortex produces corticospinal facilitation only for imagined movements of the left hand (Fadiga *et al.*, 1999). In our laboratory, we have previously reported similar somewhat lateralized findings in a task in which subjects are watching left and right hand movements (Aziz-Zadeh *et al.*, 2002). The lack of lateralization in the present study, however, can be most likely explained by the fact that ventral premotor areas were stimulated rather than the primary motor cortex. These two types of cortices have different control over the left and right hand, the primary motor cortex being mostly concerned with the contralateral hand and the premotor cortex being concerned with both left and right hand (Passingham, 1993). This factor may account for the differences in laterality between our rTMS study and the previous single pulse TMS studies.

The bilateral effect of rTMS on subjects' ability to imitate finger movements may look at first sight not in line with data from patients with apraxia, typically associated with left hemisphere lesions. Our results, however, suggest that the imitative deficit we induced with rTMS is at the level of goal imitation. The imitative abilities of patients with apraxia are rarely tested specifically on imitating the goal of the action. Thus, a direct comparison between the findings in apraxia studies and of the present study may be difficult. The bilateral effect reported here, however, is in line with recent fMRI data showing a bilateral activation in pars opercularis of the inferior frontal gyrus for imitation of goal-directed actions compared to imitation of actions with no visible goal (Koski *et al.*, 2002).

Another important issue to consider is whether the effect we report here is due to some aspects of motor control and motor learning that are not specific to imitation. For instance, the inferior frontal cortex is activated during sequence learning (Seitz & Roland, 1992; Hazeltine *et al.*, 1997). In our study, to maximize aspects of imitative behaviour that have to do with the process of replicating a new action, we used a large set of stimuli (160 different clips) such that in each trial the imitated action was novel in some aspects of it. The ever changing nature of our stimuli rules out that the effect reported here is due to interference in sequence learning, a type of motor learning associated with activation in inferior frontal cortex (Seitz & Roland, 1992; Hazeltine *et al.*, 1997).

Let us now address the interpretational limitations of our study. First, there is still limited understanding of the physiological consequences of TMS. This is especially relevant to the issue of the possible differential contribution of subareas within Broca's area to motor control, imitation and language, a differential contribution that is difficult to address experimentally with rTMS. Second, the anatomical intersubject variability in sulcal and gyral anatomy is also associated by anatomical variability in underlying cyto-architecture. This factor may account for differences in rTMS effect at individual level and will require further investigations in future studies, for instance combining a functional MRI activation study that guides the targeting of a brain area with repetitive TMS. In spite of these limitations, TMS remains a useful tool for cognitive neuroscientists especially because gives complementary information to imaging datasets.

To conclude, our findings suggest that Broca's area has an essential role in imitation of finger movement. This excludes the possibility that this region of the human brain is exclusively dedicated to language

processing and rather suggests an evolutionary continuity between action recognition, imitation, and language, and shared neural mechanisms for all these forms of communication between individuals. These shared neural mechanisms are likely non-inferential mechanisms of 'mirroring', creating a neural identity between the sender and the receiver of communication that grounds understanding.

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Abbreviations

fMRI, functional magnetic resonance imaging; LPO, left pars opercularis; MR, magnetic resonance; MT, motor threshold; OCC, occipital cortex; RPO, right pars opercularis; rTMS, repetitive TMS; TMS, transcranial magnetic stimulation.

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